

AD-A178 063

THE ROLE OF GRAPH-THEORETICAL INVARIANTS IN CHEMISTRY
(U) GEORGIA UNIV ATHENS DEPT OF CHEMISTRY D H ROUVRAY
06 MAR 87 TR-43 N00014-84-K-0365

1/1

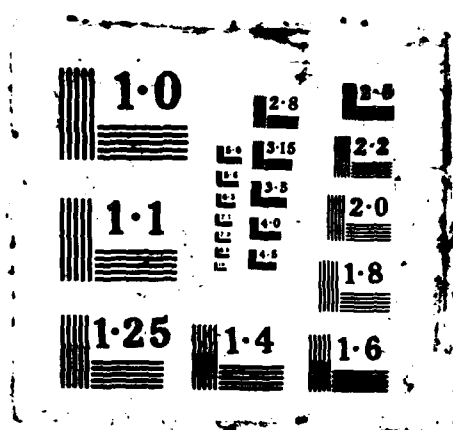
UNCLASSIFIED

F/G 12/1

NL



IND
4 5/1
DHC



Unclassified

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

(3)

AD-A178 063

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER Technical Report No. 43	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) The Role of Graph-Theoretical Invariants In Chemistry		5. TYPE OF REPORT & PERIOD COVERED
		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) D.H. Rouvray		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS University of Georgia Department of Chemistry Athens, GA 30602		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS NR051-861
11. CONTROLLING OFFICE NAME AND ADDRESS Office of Naval Research Department of the Navy Arlington, VA 22217		12. REPORT DATE 3/6/87
		13. NUMBER OF PAGES 16
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)		15. SECURITY CLASS. (of this report)
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) This document has been approved for public release and sale; its distribution is unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report) DTIC ELECTE MAR 19 1987 S D		
18. SUPPLEMENTARY NOTES To be published in <u>Congressus Numerantium</u>		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Graph Theory Invariants Topological Indices		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Graph-theoretical invariants have come to play an increasingly important role in chemistry over the past two decades. Starting from the chemical graph representing some molecular species, the most frequently derived invariants are simple numerical descriptors and polynomials. Whereas the polynomials have been used widely in the study of problems relating to chemical bonding theory, the numerical invariants have found major application in the prediction of the behavior of chemical species. The numerical descriptors, known to chemists as topological indices, are treated as inherent (OVER)		

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

Unclassified

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

OTIC FILE COPY

properties of the molecules they are employed to characterize. As such, they can be correlated against many other, experimentally measured properties of the molecules. It is from correlations of this type that predictions of the properties of unmeasured species can be made. Topological indices enjoy the twin advantages of being comparatively easy to compute and of yielding a result which is free from (experimental) error. To date, the molecular properties which topological indices have been correlated with include physical, chemical, thermodynamic, biochemical, pharmacological and toxicological properties. Over 100 different topological indices have been advanced in the chemical literature, though only a handful have so far found significant application. The results of correlative studies have in general proved to be highly encouraging, and lead us to the conclusion that the use of topological indices represents a significant advance in the prediction of the behavior of chemical substances. (Kier and Hall, 1976)

(Keywords:)

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

OFFICE OF NAVAL RESEARCH

Control N00014-84-K-0365

TECHNICAL REPORT NO. 43

THE ROLE OF GRAPH-THEORETICAL INVARIANTS IN CHEMISTRY

by
D.H. Rouvray

Prepared for publication in
Congressus Numerantium

University of Georgia
Department of Chemistry
Athens, GA 30602

March 6, 1987

Reproduction in whole or in part is permitted
for any purpose of the United States Government.

This document has been approved for public release
and sale; its distribution is unlimited.

Accession For	
NTIS	CRA&I <input checked="" type="checkbox"/>
DTIC	TAB <input type="checkbox"/>
Unannounced <input type="checkbox"/>	
Justification	
By	
Distribution /	
Availability Codes	
Dist	Avail and/or Special
A-1	



THE ROLE OF GRAPH-THEORETICAL INVARIANTS IN CHEMISTRY

D.H. Rouvray

Department of Chemistry, University of Georgia, Athens, Georgia 30602

Abstract

Graph-theoretical invariants have come to play an increasingly important role in chemistry over the past two decades. Starting from the chemical graph representing some molecular species, the most frequently derived invariants are simple numerical descriptors and polynomials. Whereas the polynomials have been used widely in the study of problems relating to chemical bonding theory, the numerical invariants have found major application in the prediction of the behavior of chemical species. The numerical descriptors, known to chemists as topological indices, are treated as inherent properties of the molecules they are employed to characterize. As such, they can be correlated against many other, experimentally measured properties of the molecules. It is from correlations of this type that predictions of the properties of unmeasured species can be made. Topological indices enjoy the twin advantages of being comparatively easy to compute and of yielding a result which is free from (experimental) error. To date, the molecular properties which topological indices have been correlated with include physical, chemical, thermodynamic, biochemical, pharmacological and toxicological properties. Over 100 different topological indices have been advanced in the chemical literature, though only a handful have so far found significant application. The results of correlative studies have in general proved to be highly encouraging, and lead us to the conclusion that the use of topological indices represents a significant advance in the prediction of the behavior of chemical substances.

Chemical Graph Invariants

Graph invariants have been the focus of much interest on the part of mathematicians for well over a century [1], and many different invariants have been intensively studied [2]. In the chemical domain, graph invariants have also been used for over a century, unwittingly at first and then with increasing awareness. In fact, over the past two decades, graph invariants may be said to have attained a position of some prominence in chemistry. This accomplishment is due in large measure to the now prevailing view that graph invariants represent in the hands of the chemist a valuable and useful new tool. Graph invariants are being used principally for the characterization of chemical graphs. In this context, the invariants are regarded as properties of the chemical graphs, and, by a fairly natural extension, also as properties of the molecules the graphs represent. Properties obtained by purely mathematical means, namely by applying an appropriate algorithm to the chemical graph, are usually treated like any other molecular property. They can, for instance, be correlated against other, experimentally determined properties, such as the boiling point, melting point, or refractive index. Graph invariants thus provide a convenient means of converting the structure of a molecule into a parameter that may be regarded as a property of that molecule [3].

In chemical terms, the invariants are said to characterize the molecular topology of the molecule under consideration, i.e. they yield a measure of the connectedness of the chemical graph. The invariants themselves are usually referred to as topological indices. Currently, over 100 different topological indices have been put forward in the chemical literature for the purpose of characterizing chemical graphs, though to date no more than a handful of these have found major applications [4]. Some of the indices are suitable for the characterization of specific parts of chemical graphs. The ability to do this is especially useful when dealing with molecules which have active sites or centers. Using regression analyses, indices have been correlated with a wide range of measured molecular properties [5,10], including physical (e.g. boiling point), chemical (e.g. reactivity), thermodynamic (e.g. heat of combustion), biochemical (e.g. biological degradability), pharmacological (e.g. anesthetic behavior), physiological (e.g. mutagenicity), and toxicological (e.g. toxicity) properties of species. Correlation coefficients in the region

of 0.99 are fairly commonplace for physicochemical properties, whereas for the more biologically oriented properties a coefficient of around 0.95 is usually regarded as excellent.

The reason for the extraordinary range of properties correlated and predicted using topological indices is that the indices are reflecting a very fundamental molecular parameter. This parameter is the connectedness of the graph or, in chemical terminology, the topology of the molecule. In a large number of cases, it is this parameter which appears to govern molecular behavior. Moreover, it is now well-known [11] that topological indices provide a measure of both the size and shape of the molecules they represent. By size in the present context is meant the volume of the molecule, and by shape we understand the distribution of that volume in 3-space. Although the physicochemical properties of molecular species are frequently largely determined by these factors, biological properties are in general dependent on several different factors. This makes biological properties more difficult to correlate using only topological indices; the generally lower correlation coefficients for a number of biological properties bear witness to this fact. Many biological responses are triggered by the interaction of specific parts of a molecule with some biological receptor. In such cases, only the part of the molecule actually interacting -- rather than the molecule as a whole -- is of prime importance. Thus, indices which characterize specific molecular sites are of especial value for a number of biological correlations.

In general, topological indices work best when they are employed for correlations of related series of molecules, e.g. for the members of homologous series. Within such series, equivalent chemical bonds in the various members are more or less identical in the sense that they possess closely similar force constants. Whenever this condition holds, the members of the series are said to exhibit bond transferability. Much of the early correlative work was carried out on homologous series, such as the alkane (C_nH_{2n+2}) series [12-14]. More recently, correlations have been obtained for a variety of other series, such as those based on nitrogen-containing heterocyclic compounds [15]. For the indices to function as molecular descriptors, they must be able to provide characterizations of many different classes of graph of chemical interest. Thus, they must be able to describe trees and especially the extent of branching in them, as well as reflect

the presence of multiple edges (multiple bonds), cycles (rings), and weighted edges (heteroatoms). Ideally, topological indices should yield unique characterizations of these graphs. Although there is no unique index currently available -- and the discovery of such an index seems highly unlikely, -- a number of them are highly discriminating for classes of graphs of chemical interest [16]. The nonuniqueness is not as troublesome to chemists as it might seem, since nonisomorphic graphs possessed of identical indices are frequently associated with molecules displaying roughly comparable properties.

The Wiener Index

The first of the topological indices, put forward by Wiener [12] in 1947, is known to reflect principally the size of a molecule, though some allowance is also made for its shape [17]. The Wiener index, $W(G)$, is defined as one half the sum of the elements in the distance matrix of the chemical graph in question, i.e.

$$W(G) = \frac{1}{2} \sum_{i=1}^n \sum_{j=1}^n d_{ij} \quad , \quad (1)$$

where n is the number of non-hydrogen atoms in the chemical graph. Hydrogen atoms are usually excluded from chemical graphs as they are not structure-determining; they can readily be added in if and when required. Several formulas for calculating $W(G)$ values have been cited by Rouvray [18]; a closed, analytical expression for the general tree was recently published by Canfield et al. [19]. The index has been used primarily in correlating a wide range of the physicochemical properties of hydrocarbon molecules [14]. To a very limited extent, the index has also found application in the more biologically oriented sciences [20]. As typical examples of the type of correlations obtained, we show in Figure 1 correlations on linear and logarithmic scales for the boiling points of unbranched alkane (C_nH_{2n+2}) molecules. Note that, even on the logarithmic scale, the plot is not a straight line (vide infra).

Some of the greatest successes of the Wiener index have been achieved with very large systems, such as polymeric or solid state systems. One approach, due to Mekenyan et al. [21], made use of a normalized Wiener

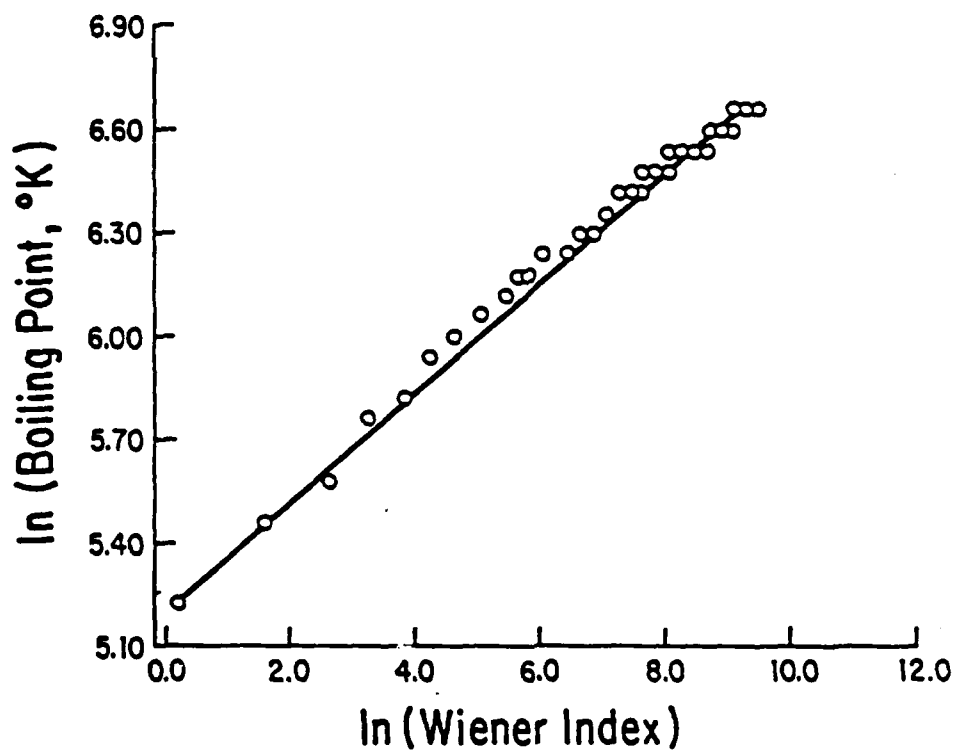
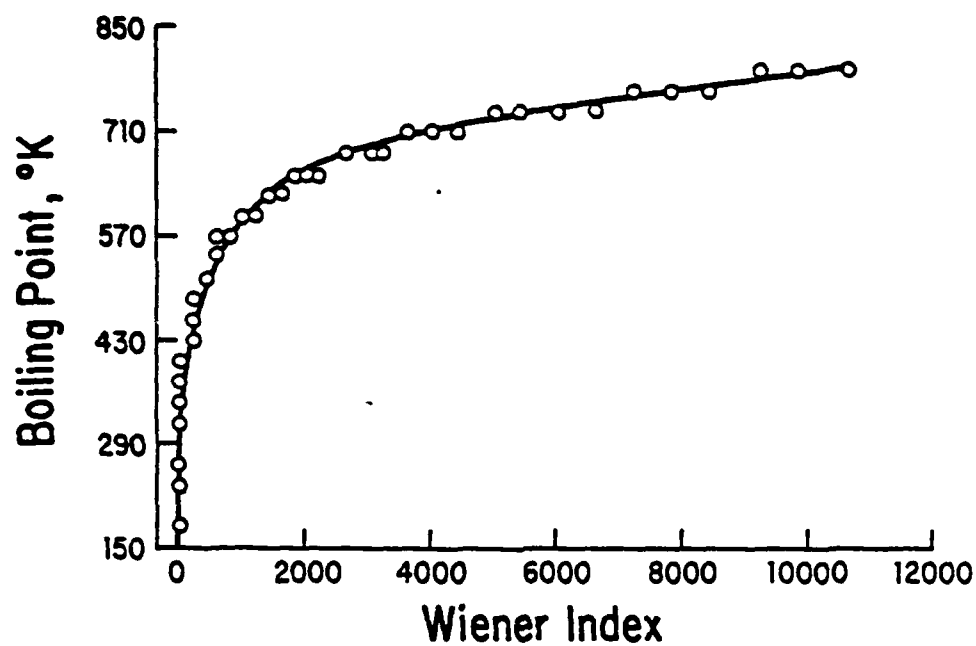


Figure 1. Plots on linear and logarithmic scales of the Wiener index, $W(G)$, against the boiling point of the first forty unbranched alkane species.

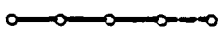
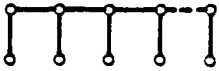



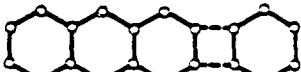
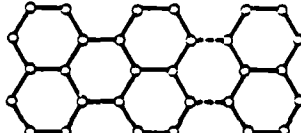
Polymeric System	Wiener Index
	$\frac{1}{6}(n^3 - n)$
	$\frac{1}{12}(n^3 + 6n^2 - 10n)$
	$\frac{1}{2}(n^3 + 3n^2 - 4n)$
	$\frac{1}{8}n^3$
	$\frac{1}{18}(2n^3 + 9n)$
	$\frac{1}{12}(n^3 + 3n^2 + 2n - 12)$
	$\frac{1}{30}(2n^3 + 235n - 1080)$

Figure 2. Closed expressions for the values assumed by the Wiener index, $W(G)$, in various monomeric units.

index which took finite values for infinite chains of monomeric units. Closed expressions for the Wiener index of a number of such chains are shown in Figure 2. The indices were normalized by dividing by a polynomial of the same degree. Substitution of the normalized $W(G)$ values into appropriate regression equations afforded good estimates of the properties of the infinite chains [21]. Moreover, Rouvray and Pandey [22] have demonstrated that $W(G)$ can provide useful information on the mean configuration adopted by long alkane molecules at their boiling point. Using the concept of fractal dimensionality, they were able to show that the ratios of slopes in the logarithmic plot in Figure 1 should tend to the limit value of 0.6 for unbranched chains of infinite length. As this limit is indeed approached in practice, it becomes possible to estimate the mean configuration of the molecules [15]. In solid state lattices, favored vacancy positions can be determined by calculating differences

in $W(G)$ for the structure under study and some ideal reference structure [23]. Minimization of these differences leads to the structure actually adopted. This work could have important applications in the modeling of crystal growth processes, gas absorption in solids, catalytic reactions, and the optimal positioning of vacancies in crystal lattices.

The Hosoya Index

After Wiener's early work, the next major advance came in 1971 when Hosoya [24] put forward his index. The index is defined by the equation:

$$Z(G) = \sum_{k=0}^{[n/2]} p(G, k), \quad (2)$$

where $p(G, k)$ is the number of ways in which k disconnected K_2 graphs can be imbedded in the chemical graph G as subgraphs, and $[n/2]$ represents the maximal value assumed by k . From the definition it follows that $p(G, 0)$ will be unity, $p(G, 1)$ the number of edges in G , and $p(G, n/2)$ the number of 1-factors (Kekulé structures) in G . The index has been used primarily to model the properties of hydrocarbon species. A number of empirical rules have been advanced [25] which prescribe the extent of the lowering of the boiling point with increasing branching in a variety of alkane species. Gutman [26] has also shown that $Z(G)$ is suitable for modeling the well-known alternations in the boiling points of substituted alkane species. Finally, it has been demonstrated [27] that $\log Z(G)$ values can model both the diminution of the rotational degree of freedom of molecules associated with increasing branching, and the decrease in the partition function arising from overcrowded molecular conformations.

Hosoya [28] also introduced the $Z(G)$ polynomial defined as follows:

$$P(G; x) = \sum_{k=0}^{[n/2]} p(G, k) x^k. \quad (3)$$

Both the Hosoya index and polynomial are closely related to several other graph invariants in chemistry. For instance, $Z(G)$ is linked with the characteristic polynomial, $C(x)$, of a given graph. In the case of trees, the relationship assumes the form [24, 29]:

$$C_T(x) = \sum_{k=0}^{[n/2]} (-1)^k p(T,k) x^{n-2k}, \quad (4)$$

whereas for cyclic graphs some additional terms appear in equation (4). The characteristic polynomial yields via its eigenvalues the energy levels of the molecule under study [30]. Moreover, the values assumed by $Z(G)$ for linear molecules (path graphs) form members of the Fibonacci series while corresponding values for monocycles form members of the Lucas series. Broadly speaking, polynomial invariants have been employed in chemistry for three major purposes, viz. (i) study of the bonding in aromatic and other organic molecules based on simple one-electron models; (ii) correlation of a variety of physicochemical properties of molecules; and (iii) investigation of the extent of branching in molecular species and the chemical consequences that may be drawn therefrom. For a full account of the manifold uses of polynomials in chemistry, the interested reader is referred to the review by Gutman [31].

Molecular Connectivity Indices

The most successful topological index published to date in terms of its number of applications is the molecular connectivity index of Randić. The index was put forward in 1975 and was originally intended to characterize the branching in alkane (C_nH_{2n+2}) species [32]. More recently, it has been shown to have numerous applications in both the physical and biological sciences [5,9,10]. The index is based on the notion of edge types in chemical graphs and is defined by the general relation:

$$\chi(G) = \sum_{\text{edges}} (v_i v_j)^{-1/2}, \quad (5)$$

where the summation extends over all the edges of G , and v_i and v_j are the degrees of a pair of neighboring vertices connected by the edge $\{i,j\}$. This index is now more correctly referred to as ${}^1\chi(G)$, since its early successes led to the introduction of a whole range of other $\chi(G)$ indices, now designated as ${}^0\chi(G)$, ${}^1\chi(G)$, ${}^2\chi(G)$, etc. for paths of length zero, one, two, etc. The generalized index, ${}^h\chi(G)$, may thus be defined for trees by the equation:

$$h\chi(G) = \sum_{\pi} (v_1(\pi)v_2(\pi) \dots v_{h+1}(\pi))^{-1/2}, \quad (6)$$

where π extends over all paths of length h , and $v_i(\pi)$ denotes the valence of the i th vertex on path π , with $1 \leq i \leq h+1$. The $h\chi(G)$ index is, of course, also derivable by exponentiation to the power h of the adjacency matrix of G . Indices with differing h values will assign different weightings to the contributions made by primary (CH_3), secondary (CH_2), tertiary (CH), or quaternary (C) carbon atoms in hydrocarbon and other species.

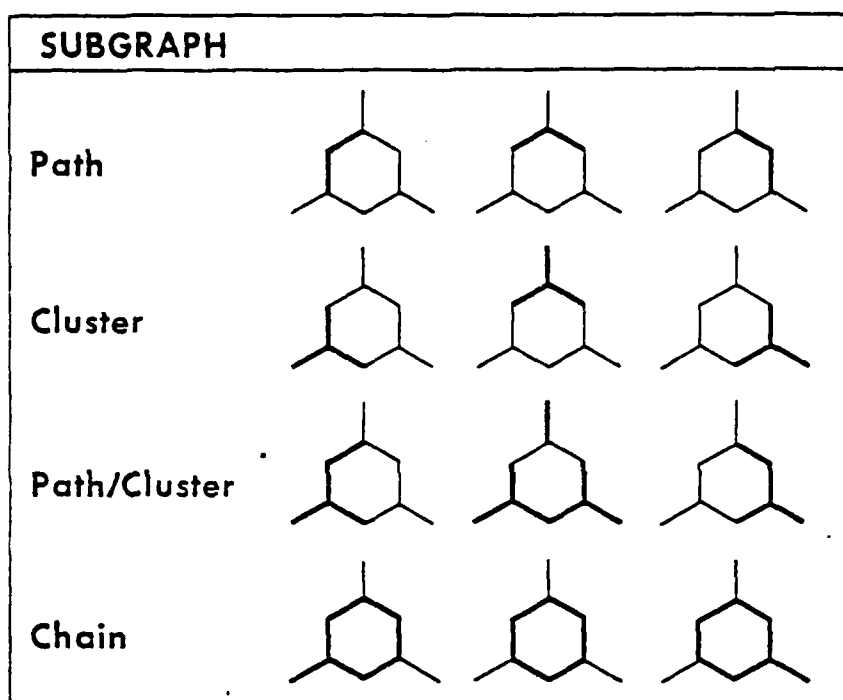


Figure 3. Illustration of the various types of subgraph used in calculating Randić molecular connectivity indices.

As part of the generalization process, the molecular connectivity index was defined for a variety of subgraphs of G other than edges. The subgraphs chosen for the definition of G are now referred to as paths, clusters, path/clusters, and chains; these are all illustrated in Figure 3. By allowing for such subgraphs, the most general form of the index may be written as:

$$h\chi_t(G) = \sum_{k=1}^{n_h} \prod_{i=1}^{h+1} (v_i)_k^{-1/2}, \quad (7)$$

where h is the number of edges in the subgraphs of G used to calculate

the index, t is the type of subgraph used (Figure 3), n_h is the number of subgraphs of type t having h edges, and the index k extends over all the n_h subgraphs. As it is of great importance to be able to deal with molecular species containing so-called heteroatoms, i.e. atoms other than carbon or hydrogen, a further generalization of the index was made by Kier and Hall [33]. The valencies of heteroatoms were assigned on the basis of their electronic charge; this led to an appropriate weighting of the graph vertices. Molecules containing any kinds of atom can thus be treated by means of molecular connectivity indices.

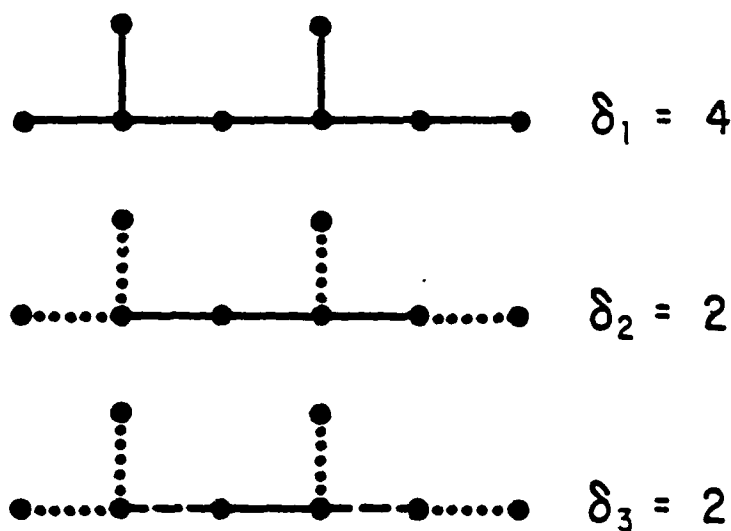
To specify even the principal applications of molecular connectivity indices would be a substantial undertaking. The authors of well over 100 papers have made use of these indices for the correlation and prediction of a very wide variety of physical, chemical, and biological properties. In the physical context mention may be made of properties such as the boiling point, solubility, density, heat of vaporization, and partition coefficient. In the more chemical realm, the properties correlated include the heat of combustion, heat of formation, chromatographic retention time, taste, and soil sorption. Examples from the biological sphere include narcotic activity, mutagenicity, toxicity, biodegradability, and bioconcentration factors. Reviews covering the principal applications of these indices have been published by Kier and Hall [9], Sabljic and Trinajstić [5], and Rouvray [10]. The surprisingly good correlations obtained with numerous biological properties open up the possibility of employing the indices in several novel roles embracing areas such as the design of new drugs, and the prediction of the toxicity of new chemical substances -- which are currently being generated at the rate of several hundred thousand per annum -- before they are actually synthesized.

Special Purpose Indices

A number of topological indices have been developed for the purpose of resolving special problems. Such indices are usually designed with a specific purpose in mind. An example of this type of index is provided by those indices used to characterize a given portion of a molecule rather than the molecule as a whole. This means in graph-theoretical terms characterizing certain of the vertices in the chemical graph of the molecule. These indices have proven to be very valuable in the investigation of

physical and chemical interactions in which one particular site in a molecule is highly active and the rest of the molecule is relatively inactive. This is normally the case when a drug molecule interacts with a biological receptor in a living organism to produce some biological response. Only one part of the molecule is capable of fitting into the receptor and triggering the appropriate response. We now discuss two examples of such special purpose indices. One of these was introduced to describe the extent of branching present in alkane species (which have tree graphs of maximal valence four), and the other to characterize each of the individual atoms in polycyclic aromatic hydrocarbons (which have polyhex graphs).

The Balaban Centric Index



$$C(G) = 4^2 + 2^2 + 2^2 = 24$$

Figure 4. Illustration of the derivation of the Balaban centric index for the graph of the molecule of 2,4-dimethylhexane.

The first special purpose index was introduced to characterize certain alkane molecules commonly used as fuel molecules in internal combustion engines. These molecules have been assigned octane number ratings which provide a measure of the anti-knock characteristics of the fuel in question. Octane numbers are known to depend on the amount of branching present in the molecule; the more branched a given fuel molecule is, the less likely

it will be to self-ignite or 'knock' upon sudden compression in air. Therefore, the more branching present in the molecule the better it will function as a fuel. To quantify the extent of branching present, Balaban and Mořoc [33,34] made use of the concept of normalized centric indices. The index used in their study can be defined as:

$$B(G) = \frac{1}{2} \left[\sum_i \delta_i^2 - 2n + \frac{1}{2}(1 - (-1)^n) \right], \quad (8)$$

where n is the number of carbon atoms in the molecule. The summation of the δ_i^2 terms represents the centric index for the molecule and the remaining terms in equation (8) represent the value of the index for a path graph on n vertices. By subtracting the two latter terms from the summation, the index is said to be normalized. The δ_i terms are obtained by successively pruning from the chemical graph all vertices of degree one. The δ_i terms are then squared and added to yield the index, as illustrated in Figure 4. In linear regression analyses with their octane numbers, the centric indices for various isomeric heptane (C_7H_{16}) and octane (C_8H_{18}) species yielded high correlation coefficients (on the order of 0.98).

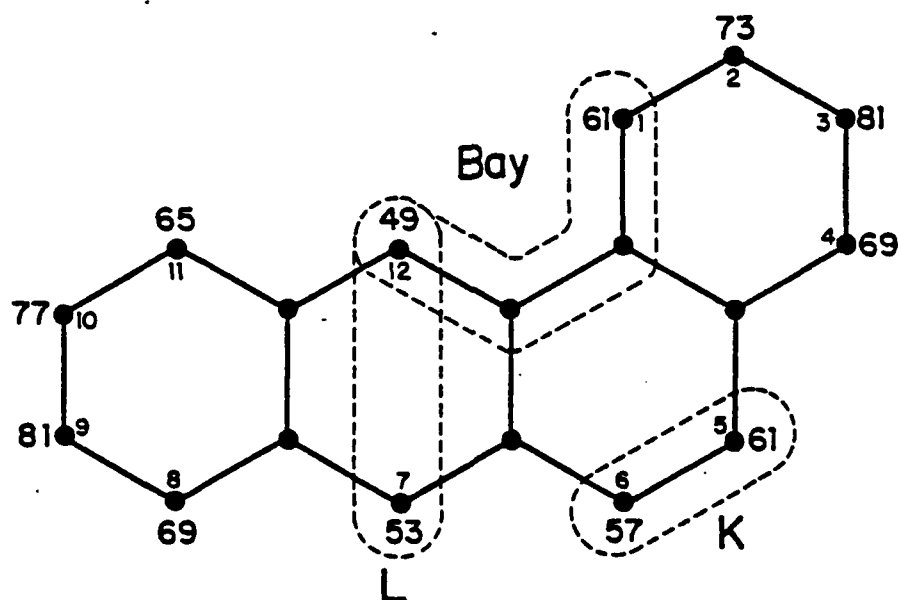


Figure 5. Illustration of the graph of the molecule of benz[a]anthracene showing active and inactive regions.

The second special purpose index we discuss was originally introduced by Randić [35] and more recently adapted by Seybold [36] to the study of

molecules having polyhex graphs. Such molecules are referred to by chemists as arenes or polycyclic aromatic hydrocarbons. It has been known for over 50 years that a number of these molecules are carcinogenic, i.e. they cause cancerous lesions in experimental animals and humans. The question was posed whether the extent of the carcinogenicity of these molecules could be correlated with a specialized index. Early on it was realized that certain parts of these molecules were active and others relatively inactive. The molecules were accordingly divided up into various regions, as shown in Figure 5. For such a molecule to be carcinogenic, the K and bay regions need to be active while the L region must be inactive. The index employed is now referred to as the atomic index as it characterizes each of the atoms in the molecule. The index is defined by the relationship:

$$S(G) = \sum_{j=1}^n d_{ij} \quad (9)$$

and thus equals the sum of the shortest paths from every vertex in the graph to vertex i . This sum, of course, is obtained by summing the d_{ij} elements of the distance matrix, $D(G)$, for the graph in question along either the i th row or column. The index provides a measure of the connectedness of each atom in the molecule, a low value of $S(G)$ indicating a more connected atom. The more connected an atom in a molecule, the easier it will be for electrons to flow to and from that atom and hence the more likely it is to be a reactive atom. This fact is confirmed in the case of the molecule of benz[a]anthracene shown in Figure 5. The $S(G)$ indices have been calculated for atoms of interest, and it is evident that those with the lowest values of the index are precisely those that fall within the active K and bay regions. Thus, even very simple indices, such as $S(G)$, can often provide remarkably penetrating insights into the inner workings of complex phenomena, such as carcinogenesis. By means of this index, Seybold [36] was able to predict which arene molecules would be carcinogenic in experimental animals, and also obtain reliable estimates of the degree of carcinogenicity of each of them.

Acknowledgments

This project was partially supported by funding from the United States Office of Naval Research. The author thanks the Department of Mathematics

at Florida Atlantic University for inviting him to give a plenary lecture having the same title as this article.

References

1. N.L. Biggs, E.K. Lloyd and R.J. Wilson, Graph Theory: 1736-1936, Clarendon Press, Oxford, 1976.
2. R.C. Bringham and R.D. Dutton, A compilation of relations between graph invariants, Networks 15, 73-107 (1985).
3. M. Randić, Nonempirical approach to structure-activity studies, Int. J. Quant. Chem., Quant. Biol. Symp. 11, 137-153 (1984).
4. D.H. Rouvray and C. Raychaudhury, The taxonomy of topological indices, J. Comput. Chem., in press.
5. A. Sabljic and N. Trinajstić, Quantitative structure-activity relationships: the role of topological indices, Acta Pharm. Jugosl. 31, 189-214 (1981).
6. A.T. Balaban, I. Mořoc, D. Bonchev and O. Mekenyan, Topological indices for structure-activity correlations, Topics Curr. Chem. 114, 21-55 (1983).
7. D. Bonchev, Information-Theoretic Indices for Characterization of Chemical Structures, Research Studies Press (Wiley), Chichester, U.K., 1983.
8. D.H. Rouvray, Should we have designs on topological indices? in R.B. King (ed.) Chemical Application of topology and Graph Theory, Elsevier, Amsterdam, 1983, pp. 159-177.
9. L.B. Kier and L.H. Hall, Molecular Connectivity in Structure-Activity Analysis, Research Studies Press (Wiley), Chichester, U.K. 1986.
10. D.H. Rouvray, The prediction of biological activity using molecular connectivity indices, Acta Pharm. Jugosl., in press.
11. D.H. Rouvray, Predicting chemistry from topology, Scientific American, 254, 40-47 (1986).
12. H. Wiener, Structural determination of paraffin boiling points, J. Amer. Chem. Soc. 69, 17-20 (1947).
13. L.I. Stiel and G. Thodos, The normal boiling points and critical constants of saturated aliphatic hydrocarbons, Amer. Inst. Chem. Eng. J. 8, 527-529 (1962).
14. D.H. Rouvray and B.C. Crafford, The dependence of physicochemical properties on topological factors, S. Afr. J. Sci. 72, 47-51 (1976).

15. T.W. Schultz, L.B. Kier and L.H. Hall, Structure-toxicity relationships of selected nitrogenous heterocyclic compounds. III. Relations using molecular connectivity, Bull Environm. Contam. Toxicol. 28, 373-378 (1982).
16. M. Randić, On molecular identification numbers, J. Chem. Inf. Comput. Sci. 24, 164-175 (1984).
17. I. Moţoc and A.T. Balaban, Topological indices: Intercorrelations, physical meaning, correlational ability, Rev. Roumaine Chim. 26 593-600 (1981).
18. D.H. Rouvray, The role of the topological distance matrix in chemistry, in N. Trinajstić (ed.) Mathematics and Computational Concepts in Chemistry, Ellis Horwood Publishers, Chichester, U.K., 1986, chap. 25, pp. 295-306.
19. E.R. Canfield, W.R. Robinson and D.H. Rouvray, Determination of the Wiener molecular branching index for the general tree, J. Comput. Chem. 6, 598-609 (1985).
20. M. Medic-Sarić, D. Maysinger and M. Movrin, Nitroxoline Mannich bases: relationship between chromatographic R_M values, Wiener's number and antibacterial activities, Acta Pharm. Jugosl. 33, 199-208 (1983).
21. O. Mekenyan, S. Dimitrov and D. Bonchev, Graph-theoretical approach to the calculation of physicochemical properties of polymers, Eur. Polym. J. 19, 1185-1193 (1983).
22. D.H. Rouvray and R.B. Pandey, The Fractal nature, graph invariants, and physicochemical properties of normal alkanes, J. Chem. Phys. 85, 2286-2290 (1986).
23. D. Bonchev, O. Mekenyan and H.-G. Fritsche, A topological approach to crystal vacancy studies. I. Model crystallites with a single vacancy, Phys. Stat. Sol. 55A 181-187 (1979).
24. H. Hosoya, Topological index: A newly proposed quantity characterizing the topological nature of structural isomers of saturated hydrocarbons, Bull. Chem. Soc. Japan 44, 2332-2339 (1971).
25. H. Hosoya, K. Kawasaki and K. Mizutani, Topological index and thermodynamic properties. I. Empirical rules on the boiling point of saturated hydrocarbons, Bull Chem. Soc. Japan 45, 3415-3421 (1972).
26. I. Gutman, A regularity for the boiling points of alkanes and its mathematical modeling, Z. Phys. Chem., in press.
27. H. Narumi and H. Hosoya, Topological index and thermodynamic properties. II. Analysis of the topological factors on the absolute entropy of

acyclic saturated hydrocarbons, Bull. Chem. Soc. Japan 53, 1228-1237 (1980).

28. H. Hosoya, Graphical enumeration of the coefficients of the secular polynomials of the Hückel molecular orbitals, Theor. Chim. Acta 25, 215-222 (1972).
29. H. Hosoya, K. Hosoi and I. Gutman, A topological index for the total π -electron energy: Proof of a generalized Huckel rule for an arbitrary network, Theor. Chim. Acta 38, 37-47 (1975).
30. R.B. Mallion, Some chemical applications of the eigenvalues and eigenvectors of certain finite, planar graphs, in R.J. Wilson (ed.) Applications of Combinatorics, Shiva Publishing, Nantwich, U.K., 1982, chap. 7, pp. 87-114.
31. I. Gutman, Polynomials in graph theory, in D. Bonchev (ed.) Annals of Mathematical Chemistry, Abacus Press, Tunbridge Wells, U.K., 1987, in press.
32. M. Randić, On characterization of molecular branching, J. Amer. Chem. Soc. 97, 6609-6615 (1975).
33. A.T. Balaban, Chemical graphs XXXIV. Five new topological indices for the branching of tree-like graphs, Theor. Chim. Acta 53, 355-375 (1979).
34. A.T. Balaban and I. Moçoc, Chemical graphs XXXVI. Correlations between octane numbers and topological indices of alkanes, Math. Chem. 5, 197-218 (1979).
35. M. Randić, Characterization of atoms, molecules and classes of molecules based on path enumerations, Math. Chem. 7, 5-64 (1979).
36. P.G. Seybold, Topological influences on the carcinogenicity of aromatic hydrocarbons. I. The bay region geometry, Int. J. Quant. Chem., Quant. Biol. Symp. 10, 95-101 (1983).

END

4-87

DTIC